BUCHWALD-HARTWIG CROSS COUPLING OF 13α-ESTRONE

Dávid Szemerédi[1], Ildikó Bacsa[1], János Wölfling[1], Gyula Schneider[1], Erzsébet Mernyák[1]

[1]Department of Organic Chemistry, University of Szeged, Dóm tér 8, H-6720, Szeged, Hungary
e-mail: bobe@chem.u-szeged.hu

Abstract
Use of catalysts and alternatives of traditional heating are important part of environmentally-friendly processes and sustainable chemistry. Here we aimed to develop a suitable method for Buchwald-Hartwig amination of 13α-estrone by microwave assisted synthesis.

Introduction
Transition-metal-catalyzed cross-coupling reactions (CUAAC[1], Sonogashira[2]) were recently published on hormonally inactive 13α-estrane core. Microwave assisted Buchwald-Hartwig reactions are described on small compounds[3], but there is no example in the literature for larger molecules.

Experimental
Reactions were carried out in CEM Discover microwave reactor. Crude mixtures were purified and novel compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy measurements.

Results and discussion
First we optimized the reaction conditions: solvent, applied base, temperature and palladium source. With the optimal conditions in hand we carried out coupling reactions of different amines (Figure 1.).

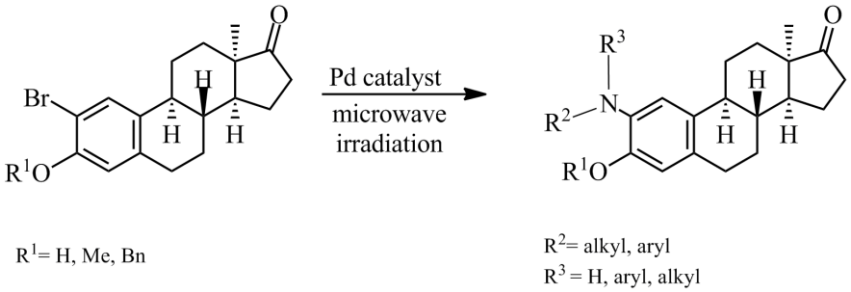

Figure 1. General method for Buchwald-Hartwig cross-coupling of 13α-estrone

Conclusion
Novel microwave assisted method was developed for Buchwald-Hartwig coupling of steroidal compound and successfully expanded to a range of substituted amines.

Acknowledgements
The authors are grateful for financial support from the Hungarian Scientific Research Fund (OTKA K113150). This project has been supported by the GINOP 2.3.2-15-2016-00038 grant of the Hungarian National Research, Development and Innovation Office (NKFIH).

References
[1] Szabó J., Bacsa I., Wölfling J., Schneider G., Zupkó I., Varga M., Herman B.E., Kalmár L., Szécsi M., Mernyák E. Journal of Enzyme Inhibition and Medicinal Chemistry 2016, 31, 574−579.

[2] Bacsa I., Jójárt R., Wölfling J., Schneider G., Herman B.E., Szécsi M., Mernyák E. Beilstein Journal of Organic Chemistry, 2017, 13, 1303-1309.
[3] Tundel R. E., Anderson K. W., Stephen L. Buchwald S. L. J. Org. Chem. 2006, 71, 430−433.